Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

4,4'-oxydi(benzenesulphonohydrazide)

EC Number: 201-286-1
CAS Number: 80-51-3

CLH-O-0000006843-68-01/F

Adopted

17 September 2020

17 September 2020

CLH-O-0000006843-68-01/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **4,4'-oxydi(benzenesulphonohydrazide)**

EC Number: **201-286-1**

CAS Number: **80-51-3**

The proposal was submitted by **Germany** and received by RAC on **26 July 2019.**

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

Germany has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **12 August 2019**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **11 October 2019**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Beata Peczkowska**

Co-Rapporteur: **Riitta Leinonen**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **17 September 2020** by **consensus**.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	4,4'-oxydi(benzenesulphonohydrazide)	201-286-1	80-51-3	Self-react. D Aquatic Chronic 1	H242 H410	GHS02 GHS09 Dgr	H242 H410		M=1	
RAC opinion	TBD	4,4'-oxydi(benzenesulphonohydrazide)	201-286-1	80-51-3	Self-react. D Aquatic Acute 1 Aquatic Chronic 1	H242 H400 H410	GHS02 GHS09 Dgr	H242 H410		M=1 M=1	
Resulting Annex VI entry if agreed by COM	TBD	4,4'-oxydi(benzenesulphonohydrazide)	201-286-1	80-51-3	Self-react. D Aquatic Acute 1 Aquatic Chronic 1	H242 H400 H410	GHS02 GHS09 Dgr	H242 H410		M=1 M=1	

GROUNDS FOR ADOPTION OF THE OPINION

RAC General Comment

4,4'-oxydi(benzenesulphonohydrazide) (OBSH) is used in polymers and for the manufacture of plastic products and rubber products. The substance is currently not listed in Annex VI of the CLP Regulation.

RAC evaluation of physical hazards

Summary of the Dossier Submitter's (DS) proposal

4,4'-oxydi(benzenesulphonohydrazide) (OBSH) is an odourless fine white crystalline powder at 20°C and 101.3 kPa. The substance decomposes at 155°C and above, therefore the melting/freezing point nor boiling point have been identified.

Explosivity

In a standard EEC A.14 study (BAM, 1992), the substance showed explosive properties as it was found to be sensitive to impact (test of mechanical sensitivity with respect to shock).

Screening procedures have been used which shows that OBSH has chemical groups present in the molecule which are associated with explosive or self-reactive properties with reference to the screening procedures in Appendix 6 of the UN-MTC (Tables A6.1 and A6.3) Secondly, the oxygen balance (-116) identifies the material to be a potential explosive, as it is greater than the limit value of -200.

The traditional aspects of explosive properties, such as detonation, deflagration and thermal explosion, are incorporated in the decision logic in Figure 2.8.1 of the CLP Regulation. Consequently, the determination of explosive properties as prescribed in the hazard class explosives needs not to be conducted for self-reactive substances and mixtures (See below).

Flammable solids

In a standard A.10 study (BAM, 1992), the substance could be ignited and a flameless combustion along 100 mm in less than 45 seconds was measured.

A substance (non-metal powder) is classified as a flammable solid when the burning time is less than 45 seconds or the burning rate is more than 2.2 mm/s, by using UN Test N.1 of the UN RTDG, Manual of Tests and Criteria.

The description of the methods A.10 and UN Test N.1 and the determination of the burning time are comparable, therefore the study should be considered to be valid. However, explosives, organic peroxides, self-reactive substances and mixtures as well as pyrophoric or oxidising solids should not be considered for classification as flammable solids since flammability is an intrinsic hazard in these classes. Consequently, the classification criteria of flammable solids need not be applied for self-reactive substances and mixtures (see below).

Self-reactive substances

Self-reactive properties of 4,4'-oxydi(benzenesulphonohydrazide) have been tested according to UN Test Series A to H in Part II of the UN RTDG, Manual of Tests and Criteria (BAM, 1992).

DSC showed an exothermic decomposition reaction with an energy release of 1042 J/g starting at 132 °C. In addition, the substance is explosive in the sense of EEC Method A.14, due to six positive results using BAM Fallhammer (mass 10 kg, drop height 40 cm).

The DS concluded that according to the classification principles given in the decision logic in Figure 2.8.1 of CLP, 4,4'-oxydi(benzenesulphonohydrazide) warrants classification as a self-reactive substance of Type D.

Pyrophoric solids

OBSH is known to be stable in contact with air at room temperature for prolonged periods of time (days) and hence, the classification procedure does not need to be applied.

Self-heating substances

The study does not need to be conducted because the substance undergoes exothermic decomposition at a temperature below or equal to 140°C.

Substances which in contact with water emit flammable gases

The study does not need to be conducted because the organic substance does not contain metals or metalloids and hence, the classification procedure does not need to be applied.

Oxidising solids

The study does not need to be conducted, no additional classification as oxidizing is required for explosive substances.

Organic peroxides

The study does not need to be conducted because the substance does not fall under the definition of organic peroxides according to GHS and the relevant UN Manual of tests and criteria.

In conclusion, the classification of 4,4'-oxydi(benzenesulphonohydrazide) as self-reactive substance Type D is proposed by the DS. The DS do not propose to classify 4,4'-oxydi(benzenesulphonohydrazide) for the hazard classes of explosives, flammable solids, pyrophoric solids, self-heating substances, substances which in contact with water emit flammable gases, oxidising solids, organic peroxides.

Comments received during consultation

No comments received.

Assessment and comparison with the classification criteria

4,4'-oxydi(benzenesulphonohydrazide) is a compound of the type of aromatic sulfohydrazides (-SO_2-NH-NH_2) known as self-reactive substances (according to section 2.8.1 of the Guidance on the Application of the CLP Criteria, Version 5.0 – July 2017).

Based on the result of differential scanning calorimetry (DSC) an exothermic decomposition reaction with an energy release of 1042 J/g, 4,4'-oxydi(benzenesulphonohydrazide) meets the definition of self-reactive substances (according to CLP Regulation, Annex I, 2.8.1.1) as thermally unstable solid substance liable to undergo a strongly exothermic decomposition.

The self-reactive properties of 4,4'-oxydi(benzenesulphonohydrazide) tested (BAM, 1992, results provided in confidential Annex of CLH report) according to UN Test Series A to H described in Part II of the UN RTDG, Manual of Tests and Criteria, fulfil the criteria for classification given in the decision logic in Figure 2.8.1 of CLP Regulation as follows:

- propagation of detonation - a test of UN Test Series A was not performed what was justified by the result "No" obtained from the explosive power test (F.3 BAM Trauzl test)

and "Low" result obtained from test E.2 (Dutch pressure vessel test (DPVT)) and "No" result obtained from test E.1 (Koenen test) – exit 1.3;
- propagation of deflagration – result "Yes, slowly" was obtained from the C.1 Time/pressure test – exit 5.2
- Effect of heating under defined confinement - result "No" was obtained from the E.1 Koenen test and result "Low" was obtained from the E.2 Dutch pressure vessel test (DPVT) – exit – 8.3/8.4.

Therefore, 4,4'-oxydi(benzenesulphonohydrazide) meets criterion "does not detonate at all, deflagrates slowly and shows no violent effect when heated under confinement" (section 2.8.2.3 (d) (ii) for classification as **self-reactive substance TYPE D**. In conclusion, RAC supports the DS's proposal to classify 4,4'-oxydi(benzenesulphonohydrazide) as **Self-react. D, (H242: Heating may cause a fire)**.

Self-reactive substances and mixtures need to be subjected to temperature control when the SADT is ≤ 55°C. The SADT is defined as the lowest temperature at which self-accelerating decomposition of a substance or mixture may occur in the packaging as used in transport, handling and storage.

Temperature control is not needed based on SADT of 4,4'-oxydi(benzenesulphonohydrazide) which is above 60°C (for a package up to 50 kg).

The traditional aspects of explosive properties, such as detonation, deflagration and thermal explosion, are incorporated in the decision logic Figure 2.8.1 of CLP. Consequently, the determination of explosive properties as prescribed in the hazard class explosives needs not to be conducted for self-reactive substances and mixtures (according to section 2.8.4.1 of Guidance on the Application of the CLP Criteria Version 5.0 – July 2017).

Self-reactive substances and mixtures should not be considered for classification as flammable solids since flammability is an intrinsic hazard in this class (according to section 2.7.3 of Guidance on the Application of the CLP Criteria Version 5.0 – July 2017).

According to CLP Annex I, 2.10.4, the classification procedure for pyrophoric solids need not be applied when experience in manufacture or handling shows that the substance or mixture does not ignite spontaneously on coming into contact with air at normal temperatures (i.e. the substance or mixture is known to be stable at room temperature for prolonged periods of time (days)).

OBSH is known to be stable in contact with air at room temperature for prolonged periods of time (days) and hence, the classification procedure for pyrophoricity does not need to be applied.

A study for self-heating substances does not need to be conducted because the substance undergoes exothermic decomposition at a temperature below or equal to 140°C.

A study for substances which emit flammable gases in contact with water does not need to be conducted because the organic substance does not contain metals or metalloids and hence, the classification procedure does not need to be applied.

According to screening procedures and waiving of testing (section 2.14.4.1.1 of Guidance on the Application of the CLP Criteria Version 5.0 – July 2017) solids that are classified as explosives should not be subjected to the testing procedures for oxidising solids. Since the screening procedure identifies 4,4'-oxydi(benzenesulphonohydrazide) to be a potential explosive (the substance contains chemical groups associated with explosive and the oxygen balance (-116) is greater than the limit value of -200) the test for oxidising solids does not need to be conducted.

According to the definition in CLP Regulation Annex I: 2.15.1 organic peroxides means liquid or solid organic substance which contain the bivalent -O-O- structure and may be considered

derivatives of hydrogen peroxide. Therefore, study for organic peroxides does not need to be conducted because the substance does not fall under the definition of organic peroxides.

In conclusion, RAC agrees with DS's proposal to classify 4,4'-oxydi(benzenesulphonohydrazide) as **self-reactive substance TYPE D (Self-react. D, H242: Heating may cause a fire)** and **not to classify the substance for the hazard classes:**

- **explosives,**
- **flammable solids,**
- **pyrophoric solids,**
- **self-heating substances,**
- **substances which in contact with water emit flammable gases,**
- **oxidising solids, and**
- **organic peroxides**.

ENVIRONMENTAL HAZARD EVALUATION

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

Summary

The Dossier Submitter (DS) proposed to classify OBSH as Aquatic Chronic 1, M=1 based on a NOEC of 0.09 mg/L for the fish *Oryzias latipes*, with an M-factor of 1 (0.01 mg/L < NOEC ≤ 1.0 mg/L). The substance was not considered rapidly degradable and to have a low potential for bioaccumulation. After the consultation comments, the DS agreed to add Aquatic Acute category 1, M=1 to their proposal based on the E_rC_{50} of 0.35 mg/L for algae.

Degradation

There was one ready biodegradability study available (OECD TG 301C, GLP). The initial test substance concentration was 100 mg/L and 30 mg/L inoculum was used. After 28 days 10.9 % degradation was observed.

Rapid hydrolysis was shown in a study according to OECD TG 111 (GLP). The study was conducted at 25 °C and the half-lives were 5.8, 7.9 and 9.2 hours for pH values 4, 7 and 9, respectively. Transformation products were not identified. Therefore, it could not be demonstrated that the transformation products do not fulfil the criteria for classification as hazardous to the aquatic environment. Based on chemical structure, potential degradation products from hydrolysis were hydrazine and 4,4'-oxybis(benzenesulfonic acid). Hydrazine has a harmonised classification as Aquatic Acute 1 and Aquatic Chronic 1 (Index number 007-008-00-3). In the response to the consultation comments, the DS also gave the half-lives at 20 and 30 °C presented in the study.

Table: *Hydrolysis half-lives of OBSH*

	pH 4	pH 7	pH 9
20 °C	23.1 h	17.2 h	13.9 h
25 °C	9.2 h	7.9 h	5.8 h
30 °C	3.76 h	3.72 h	2.46 h

The DS concluded that OBSH should be considered as not rapidly degradable for classification.

Bioaccumulation

Bioaccumulation of OBSH was evaluated according to OECD TG 305 (GLP). *Cyprinus* sp. were exposed to 0.1 and 1 mg/L of OBSH for 42 days at 25 °C. All measured concentration values were below the detection limit and no BCF could be determined. Therefore, BCF values were calculated based on the detection limit of HPLC. For 0.1 mg/L test concentration a BCF of 0.3 and for 1 mg/L a BCF of 3 were calculated, respectively.

Furthermore, a QSAR calculated BCF value was stated in the OECD SIDS Initial Assessment Report (OECD 2006). Based on the estimated log Kow of 0.08, a BCF value of 3.162 was calculated (BCFWIN v 2.15).

Acute Aquatic toxicity

Table: *Summary of relevant information on acute aquatic toxicity of OBSH* ***(the results used for classification proposal in bold)***

Method	Species	Results	Remarks	Reference
OECD TG 203	*Oryzias latipes*	**96h-LC_{50}= 74 mg/L (nominal)**	Semi-static; solvent used (DMSO); Rel.1	ECHA 2018
OECD TG 203	*Oryzias latipes*	96h-LC_{50}> 20 mg/L (nominal) 96h-LC_{50}> 6.6 mg/L (mean measured)	Semi-static; solvent used (DMF, 0.1 mL/L); Limit-test; Rel.1	ECHA 2018
OECD TG 202	*Daphnia magna*	**48h-$E_{immobilisation}C_{50}$= 15 mg/L (nominal)** 48h-$E_{immobilisation}C_{50}$= 0.69 mg/L (measured)	Static, recovery rate: 3.43 to 16.7 % OBSH; Rel.1 EC50 based on measured concentration not used because low recovery rate due to very fast hydrolysis (high tox. of one expected hydrolysis product)	ECHA 2018
OECD TG 202	*Daphnia magna*	48h-$E_{immobilisation}C_{50}$= 2.9 mg/L (measured)	Semi-static; solvent used (DMF; 0.1 mL/L); Rel.1	ECHA 2018
OECD TG 201	*Pseudokirchneriella subcapitata*	72h-ErC_{50}= 6.7 mg/L (nominal)	Static; stability test: 50% after 3h of initial level; Rel.1	ECHA 2018
OECD TG 201	*Pseudokirchneriella subcapitata*	**72h-ErC_{50}= 3 mg/L (initial measured)**	Static; solvent used, Rel.1	ECHA 2018

ECHA 2018: Registration dossier 4,4'-oxydi(benzenesulphonohydrazide) (last accessed July 2018)
DMSO = dimethyl sulfoxide
DMF = dimethylformamide

There were two acute toxicity studies for fish (OECD TG 203) available. The tests were performed with *Oryzias latipes* for 96 hours under semi-static conditions. In the first test, nominal concentrations were: control, solvent (DMSO) control, 6.3, 12.5, 25.0, 50.0, and 100.0 mg/L. The 96-hour LC_{50} was 74 mg/L based on nominal concentrations. No analytical monitoring was performed.

The second fish test was a semi-static limit test with a nominal concentration of 20 mg/L. Analytical monitoring was performed. No mortality was seen in the test. The 96-hour LC_{50} based on mean measured concentrations was > 6.6 mg/L.

For invertebrates there were two acute *Daphnia* studies (OECD TG 202) available. The first study was a static system using nominal concentrations of 0.3, 0.6, 1, 3, 5, 10, 20 and 40 mg/L. The corresponding measured concentrations were 0.05, 0.07, 0.10, 0.20, 0.38, 0.52, 0.81, and 1.37 mg/L, respectively. The 48-hour EC_{50} for immobility was 15 mg/L (nominal) and 0.69 mg/L (mean measured).

The second *Daphnia* study was semi-static and solvent DMF was used. Test concentrations were measured at the beginning of the study and 24 hrs after exposure (before renewal of test solution). The nominal concentrations were 2.0, 3.6, 6.0, 11.2, 20.0 mg/L and the corresponding mean measured concentrations in the 24-hour old test solution were 0.78, 1.24, 2.17, 3.80, and 6.50 mg/L, respectively. The geometric mean concentration during 24-hours were 1.16, 1.91, 3.39, 5.89 and 10.3 mg/L, respectively. The 48-hour EC_{50} for immobility was 2.9 mg/L (mean measured).

There were two tests available on algae. Both tests (OECD TG 201) were conducted with *Pseudokirchneriella subcapitata* under static conditions over 72 hours. In the first test, no solvent was used. The concentrations were measured at the beginning and end of the study. According to the result of analytical monitoring, OBSH was not detected in all samples at the end of the test. The nominal concentrations used in the first test were: control, 0.4, 0.9, 1.9, 4.2, and 9.3 mg/L. The result of the test was an E_rC50 of 6.7 mg/L based on nominal concentrations.

In the second test DMF was used as a solvent (0.1 mL/L). The concentrations of the test substance were measured at the beginning and end of the study. The nominal concentrations used were 0.50, 0.82, 1.40, 2.20, 3.70, 6.10, and 10.0 mg/L corresponding to initial measured concentrations of 0.45, 0.70, 1.17, 1.83, 3.11, 5.20, and 8.21 mg/L, respectively. After 72 hours, the measured concentrations were lower than 2% of the nominal. The 72-hour E_rC50 was 3 mg/L based on initial measured concentrations.

Chronic Aquatic Toxicity

Table: *Summary of relevant information on chronic aquatic toxicity of OBSH*

Method	Species	Results	Remarks	Reference
OECD TG 210	*Oryzias latipes*	**45d-$NOEC_{mortality}$ = 0.09 mg/L (arithmetic mean measured)** 45d-$NOEC_{mortality}$ = 0.10 mg/L (nominal)	Flow-through, Rel.1	ECHA 2018
OECD TG 211	*Daphnia magna*	21d-$NOEC_{reproduction}$= 2.13 mg/L (mean measured) 21d-**$NOEC_{reproduction}$= 3.80 mg/L (nominal)** 21d-$EC50_{reproduction}$= 2.48 mg/L (measured) 21d-LC50= 2.13 mg/L (measured)	Semi-static; solvent used (DMF; 0.1 mL/L); Rel.1	ECHA 2018
OECD TG 201	*Pseudokirchneriella subcapitata*	72h-NOErC= 0.9 mg/L (nominal)	Static; stability test: 50 % after 3h of initial level; Rel.1	ECHA 2018
OECD TG 201	*Pseudokirchneriella subcapitata*	**72h-NOErC= 0.82 mg/L (nominal)** 72h-NOErC= 0.7 mg/L (initial measured)	Static; solvent used, Rel.1	ECHA 2018

ECHA 2018: Registration dossier 4,4'-oxydi(benzenesulphonohydrazide) (last accessed July 2018)

DMF = dimethylformamide

There was one flow-through 45-day Early Life-Stage toxicity test available with fish, *Oryzias latipes* (OECD TG 210, GLP). DMF was used as a solvent in a concentration of 0.1 mL/L. The nominal concentrations were 0.1, 0.31, 0.98, 3.13 and 10 mg/L and the respective arithmetic mean measured concentrations were 0.09, 0.30, 1.01, 3.28 and 10.22 mg/L. The NOEC based on mortality (post hatch survival and overall survival) was 0.09 mg/L. The 45-day NOEC for hatching rate success was 1.01 mg/L. The results are based on arithmetic mean of the measured concentrations.

For invertebrates there was one long-term toxicity test on *Daphnia magna* available (OECD TG 211, GLP). This test used a solvent (0.1 mL/L DMF) and semi-static conditions. The nominal concentrations used were: 0.4, 0.85, 1.80, 3,80, and 8.00 mg/L corresponding to the time weighted mean measured concentrations of 0.229, 0.495, 1.07, 2.13, and 4.47 mg/L. Measured concentrations in the new test solutions on days 0, 7 and 14 were 81 - 93 % of the nominal concentrations. In the aged test solutions on days 1, 8 and 15 the measured concentrations were 32 - 39 % of the nominal concentrations. The peaks of the hydrolysis product were observed but not identified. The 21-day NOEC for reproduction was 2.13 mg/L based on time weighted mean measured concentrations.

The two available algae tests are described under the acute aquatic toxicity above. The two 72-hour NOE_rC values for *Pseudokirchneriella subcapitata* from these tests were 0.9 mg/L based on nominal concentrations and 0.7 mg/L based on initial measured concentrations.

Comments received during consultation

Comments were received from four Member States (MS).

One MS was of the opinion that lack of identification of hydrolysis products does not justify leaving them out of consideration and using nominal/initial measured values when evaluating the aquatic toxicity of OBSH. Consequently, the EC_{50} of 0.69 mg/L based on measured concentrations would be the lowest acute toxicity value leading to Aquatic Acute 1, M= 1 classification. Another MS supported to add acute classification to the proposed classification.

They also pointed out that when measured concentrations are available, as in for example in algae studies, results should be based on geometric mean measured concentrations, and where concentrations at the end of test are below the analytical detection limit, such concentrations shall be considered to be half that detection limit. In case of semi-static tests, it should be clarified whether the geometric mean for each renewal period has been calculated, and if the mean exposure over the whole exposure period has calculated from these data.

Although the DS in the CLH proposal had based their evaluation on nominal concentrations, they now (after receiving the comments from the consultation) agreed that test concentrations not remaining between 80 and 120% of nominal should be based on measured concentrations. They also agreed that half of the analytical detection limit should be used if the measured concentrations are below this detection limit. They also informed that for the semi-static tests described in the CLH report, the geometric mean measured concentrations included the measured concentrations for the new medium and the aged one for every renewal period. For the first algae study, the limit of quantification was 0.1 mg/L. Using the half of the LOQ the resulting mean measured concentrations would be: 0.68 – 0.46 – 0.31 – 0.21 – 0.14 mg/L (nominal: 9.3 – 4.2 – 1.9 – 0.9 – 0.4 mg/L). The E_rC_{50} based on mean measured concentrations would be 0.57 mg/L and the NOE_rC would be 0.21 mg/L.

The DS agreed that basing the classification on measured concentrations would result in an EC_{50} of 0.69 mg/L (*Daphnia magna*). The results from the algae toxicity studies based on mean

measured concentrations were in the same order of magnitude (E_rC_{50} is 0.57 or 0.35 mg/L, first and second test) and therefore they agreed to classify OBSH with Aquatic acute 1 (M=1).

The DS pointed out that the aquatic chronic classification is based on mean measured concentrations. In the relevant fish test a solvent (DMF) was used and the measured concentrations of OBSH were stable (within 80 to 120% of nominal). The 45-day NOEC = 0.09 mg/L results in Aquatic Chronic (M= 1).

One MS had concerns about the hydrolysis rate in different temperatures and its bearing on whether initial/nominal or measured values from the aquatic toxicity tests should be used. The DS presented extrapolated values at 12°C but pointed out that the extrapolation may contain remarkable uncertainties. The MS also pointed out that endpoints for length and weight are not included in the summary of the chronic toxicity test. As this is the key chronic study, these should be presented to conclude if they are more sensitive or not. According to the DS this information was not given in the report.

One MS supported the conclusion that OBSH is not rapidly degradable and not meeting the bioaccumulation criterion for classification. They also considered the first fish study with a 96-hour LC_{50} of 74 mg/L invalid because no analytical monitoring was performed during the study.

The DS agreed to consider the first fish study invalid. They also presented new calculations for the second algae study. The nominal concentrations were: 10.0 – 6.10 – 3.7 – 2.2 – 1.4 – 0.82 – 0.50 mg/L, and the mean measured concentrations (using half of the LOQ for concentrations below the LOQ): 0.81 – 0.46 – 0.35 – 0.096 – 0.076 – 0.059 – 0.047 mg/L. This resulted in an E_rC_{50} of approximately 0.35 mg/L and a NOE_rC of 0.059 mg/L.

More detailed descriptions of the studies in the CLH Report to allow proper assessment of the validity score was expected by two MS.

Assessment and comparison with the classification criteria

RAC agrees with the Dossier Submitter to consider OBSH as not rapidly degradable, based on:

- 10.9% degradation after 28 days in Ready biodegradability test – The substance is not demonstrated to be readily biodegradable
- no surface water simulation test available
- rapid hydrolysis at 25 °C; half-lives of 5.8, 7.9 and 9.2 hours for pH values 4, 7 and 9, respectively. Transformation products were not identified. Therefore, it could no demonstration that the transformation products do not fulfil the criteria for classification as hazardous to the aquatic environment.

RAC agrees with the Dossier Submitter on OBSH not being bioaccumulative:

- Bioconcentration factors 0.3 and 3 for fish are below the bioaccumulation cut-off value ≥ 500
- the estimated (KOWWIN) log K_{ow} was 0.08 and thus smaller than the cut-off log Kow of 4.

Aquatic toxicity

After the consultation comments, the DS agreed that endpoint values where test concentrations have not remaining between 80 and 120% of nominal should be based on measured concentrations. They also agreed that half of the analytical detection limit should be used if the measured concentrations are below the detection limit. Finally, they also agreed, and RAC concurs, that the first fish test with no analytical monitoring during the test was invalid.

A hydrolysis study (REACH Registration Dossier) had been presented in the CLH Report. The hydrolysis products were not identified although this is a requirement in the OECD TG 111. The hydrolysis products had not been identified in the aquatic toxicity tests either and it was therefore unclear whether the parent compound or the degradation products were responsible for the toxicity.

RAC, in line with CLP Guidance (I.4.1), agrees with the DS's view presented in the reply to the consultation comments that test concentrations not remaining between 80 and 120% of nominal should be based on measured concentrations and that half of the analytical detection limit should be used if the measured concentrations are below the detection limit. The aquatic toxicity tables below reflect this change.

Acute Aquatic Toxicity

There were relevant acute toxicity data available for fish, *Daphnia* and algae. For fish the lowest 96-hour LC_{50} based on mean measured concentrations was > 6.6 mg/L for *Oryzias latipes* in a semi-static test (OECD TG 203). For invertebrates there were two acute *Daphnia* studies (OECD TG 202) available. The lowest EC_{50} was a 48-hour EC_{50} for immobility of 0.69 mg/L (mean measured concentrations) from the static test. For algae there were two static studies available with *Pseudokirchneriella subcapitata* (OECD TG 201). In response to the consultation comments, the DS recalculated the results based on mean measured concentrations using half of the LOQ when the measured concentration was below the LOQ (CLP Guidance I.4.1). The 72-hour E_rC_{50} values were 0.57 mg/L and 0.35 mg/L based on mean measured concentrations.

***Table**: Reliable aquatic acute toxicity data on OBSH relevant for classification*

Method	Species	Test material	Results	Remarks	Reference
OECD TG 203, GLP Limit test, semi-static, renewal every 24-h	*Oryzias latipes*	OBSH	96h-LC_{50}> 6.6 mg/L (mean measured)	Solvent used (DMF 0.1 mL/L) No mortality in the test	REACH Registration Dossier
OECD TG 202, GLP Static	*Daphnia magna*	OBSH 95.3%	48-h EC_{50}: 0.69 mg/L (mm) Immobility	Static Mean measured conc. 3.43 to 16.7% of nominal (3	REACH Registration Dossier
OECD TG 202, GLP semi-static, renewal every 24-h	*Daphnia magna*	OBSH 99.3%	48-h EC_{50}: 2.9 mg/L (mm) Immobility	Solvent used (DMF 0.1 mL/L) (3	REACH Registration Dossier
OECD TG 201, GLP Static	*Pseudokirchneriella subcapitata*	OBSH 95.3%	72h-E_rC_{50}: 0.57 mg/L (mm) (1		REACH Registration Dossier
OECD TG 201, GLP Static	*Pseudokirchneriella subcapitata*	OBSH 99.3%	**72h-E_rC_{50}: 0.35 mg/L** (mm) (2 mean measured conc. after 72-h <2% of nominal	Solvent used (DMF 0.1 mL/L)	REACH Registration Dossier

REACH Registration Dossier, last modified 28.4.2020
mm=mean measured
DMF = dimethylformamide
(1 calculated by the DS in the response to the consultation comment using half of the LOQ (mean measured concentrations 0.68, 0.46, 0.31, 0.21 and 0.14 mg/L)
(2 calculated by the DS in the response to the consultation comment using half of the LOQ (mean measured concentrations 0.81, 0.46, 0.35, 0.096, 0.076, 0.059 and 0.047 mg/L)
(3 precipitation of the test substance and formation of film at the surface were observed in more than 1 mg/L but immobilisation was observed in more than 10 mg/L. Therefore, immobilization of daphnia and film formation are not related to each other (REACH Registration Dossier).

Chronic Aquatic Toxicity

There were relevant chronic toxicity data for fish, *Daphnia* and algae. For fish *Oryzias latipes* the 45-day NOEC based on mortality from the flow-through Early Life-Stage toxicity test (OECD TG 210) was 0.09 mg/L (arithmetic mean of the measured concentrations). For invertebrates there was one semi-static long-term toxicity test on *Daphnia magna* available (OECD TG 211). The 21-day NOEC for reproduction was 2.13 mg/L based on time weighted mean measured concentrations. The 72-hour NOE_rC values for *Pseudokirchneriella subcapitata* from the static studies were 0.21 mg/L and 0.059 mg/L recalculated by the DS based on mean measured concentrations using half of the LOQ when the measured concentration was below the LOQ.

Table: *Reliable aquatic chronic toxicity data on OBSH relevant for classification*

Method	Species	Test material	Results	Remarks	Reference
OECD TG 210, GLP Flow-through	*Oryzias latipes*	OBSH, 99.5-100%	45d-NOEC mortality: 0.09 mg/L (arithmetic mm)	Solvent used (DMF 0.1 mL/L) arithmetic mm conc. 80-120% of nominal	REACH Registration Dossier
OECD TG 211, GLP Semi-static, renewal on days 7 and 14	*Daphnia magna*	OBSH, 99.3%	21-d NOEC: 2.13 mg/L (mm, TWA) reproduction	Solvent used (DMF 0.1 mL/L)	REACH Registration Dossier
OECD 201, GLP Static	*Pseudokirchneriella subcapitata*	OBSH 95.3%	72-h NOE_rC 0.21 mg/L (mm) (1		REACH Registration Dossier
OECD TG 201, GLP Static	*Pseudokirchneriella subcapitata*	OBSH 99.3%	**72-h NOE_rC 0.059 mg/L** (mm) (2 mean measured conc. after 72 h <2% of nominal	Solvent used (DMF 0.1 mL/L)	REACH Registration Dossier

REACH Registration Dossier, last modified 28.4.2020
mm=mean measured
DMF = dimethylformamide
(1 calculated by the DS in the response to the consultation comment using half of the LOQ (mean measured concentrations 0.68, 0.46, 0.31, 0.21 and 0.14 mg/L)
(2 calculated by the DS in the response to the consultation comment using half of the LOQ (mean measured concentrations 0.81, 0.46, 0.35, 0.096, 0.076, 0.059 and 0.047 mg/L)

RAC concludes that the lowest value was a 72-hour NOE_rC of 0.059 mg/L (mean measured) for the algae *Pseudokirchneriella subcapitata*.

Comparison with the criteria

Acute Aquatic Toxicity

RAC is of the opinion that OBSH should be classified as Aquatic Acute 1 due to the lowest acute toxicity value 0.35 mg/L being smaller than the cut-off 1 mg/L. An M-factor of 1 is warranted (0.1 mg/L < E_rC50 ≤ 1 mg/L).

Chronic Aquatic Toxicity

RAC is of the opinion that OBSH should be classified as Aquatic Chronic 1 due to the lowest chronic toxicity value of 0.059 mg/L and the substance being not rapidly degradable (Chronic NOEC ≤ 0.1 mg/L). An M-factor of 1 is warranted (0.01 mg/L < NOEC ≤ 0.1 mg/L).

Overall, RAC agrees with the DS proposal modified after the consultation that OBSH warrants classification as **Aquatic Acute 1; H400 (M=1) and Aquatic Chronic 1; H410 (M=1)**.

There is an ongoing information request (decision on a compliance check, decision date 14/05/2020, https://www.echa.europa.eu/documents/10162/082d88da-f90c-3dcd-d3da-880d20713d93) for this substance. The classification might have to be revisited in case relevant data e.g. to identify the hydrolysis degradation products will be available.

ANNEXES:

Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).